REMARKS .

This Amendment After Final is submitted in reply to the Office Action mailed on April 6, 2006. In the Office Action, the Examiner rejected claims 13-30 and 39-51. With this Amendment After Final, claims 13-30 and 39-51 are canceled, and new claims 52-86 are added. Claims 1-12 and 31-38 were previously cancelled. Upon entry of this Amendment After Final, the above-identified application will include claims 52-86.

Though claims 13-30 and 39-51 are canceled via this Amendment After Final, Applicant continues to believe claims 13-30 and 39-51 are allowable, as originally presented in the above-identified application and also as claims 13-30 and 39-51 presently exist as of the present request to cancel claims 13-30 and 39-51. Therefore, Applicant is canceling claims 13-20, 22-28, 30, 42-62, and 64-87 without prejudice to Applicant's' right to pursue claims worded like claims 13-30 and 39-51, as originally presented or as worded subsequent to original presentation, in the above-identified application or in any continuing application that is based on the above-identified application. Furthermore, no claim cancellation made herein is related to any statutory patentability requirement unless expressly stated herein.

Claim Rejections Under the Written Description Requirement of the First Paragraph of 35 U.S.C. §112

In the Office Action, the Examiner rejected claims 13-30 and 38-51 under the first paragraph of 35 U.S.C. §112 for allegedly failing to provide an adequate written description. In support of this rejection, the Examiner stated:

> Claims 13-30 and 38-51 are rejected under 35 U:S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.
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> The instant claims are generically directed to isolated DNA and RNA which encode bovine leptin, wherein the nucleic acid molecule hybridizes to a nucleic acid sequence of SEQ ID NO:3 (or a variant thereof) under stringent hybridization conditions. However, the only such molecule disclosed in the instant specification is the nucleic acid molecule of SEQ ID NO:3 which encodes the protein of SEQ ID NO:4.

Applicant argues that "the Examiner apparently contends that disclosure of the structure (sequence) of only one molecule allegedly limits an inventor to only claiming that single molecule". Applicant's argument has been fully considered, but is not persuasive. The Examiner never stated such, nor concluded such, nor alleged such, nor implied such with regard to the written description rejection. The Examiner did point out statements of the inventor, Dr. Spurlock, which are relevant and have direct bearing on the rejection. As stated previously, Dr. Spurlock concluded

> The bottom line is that you do not know the bovine leptin sequence until you have the bovine leptin sequence. Even then, you may have variations within the species because of the genetic diversity that exists within all species populations. Some of these variations may be very important relative to the functionality of the protein. (paragraph 6 of the 1.132 Declaration filed in parent application 08/688,908).

If one of ordinary skill in the art would not know the bovine leptin sequence until they were in possession of the bovine leptin sequence, it is unclear how the instant claims meet the written description requirement when the specification provides one bovine leptin sequence, but is claiming a vast genus of molecules which have not been isolated or described. Even if one of ordinary skill in the art could use the disclosed polynucleotide sequence to hybridize to bovine polynucleotides, the skilled artisan would not know if they were in possession of bovine leptin as stated so clearly by the inventor himself.

Applicant asserts at page 13 of the response that based on the disclosure of SEQ ID NO:3, one of ordinary skill in the art would recognize that "still other related species falling within the claims are in the possession of the inventor". Applicant's assertion is noted, but is contradicted by Dr. Spurlock's own statements, as pointed out above.

Applicant argues at page 13 of the response that Example 9 of the Written Description Guidelines is analogous to the instant fact pattern. Applicant's argument has been carefully considered, but it is not persuasive. In Example 9 of the Written Description Guidelines, although hybridizing nucleic acids were not sequenced, they were isolated, expressed and "several were shown to encode proteins" which were functional. There is no such disclosure for the claimed invention. Applicant also argues that Example 10 of the Written Description Guidelines is analogous to the instant fact pattern. In Example 10, the single

disclosed species was found to be representative of the genus because reduction to practice of this species, considered along with the defined hybridization conditions and the level of skill and knowledge in the art, are sufficient to allow the skilled artisan to recognize that applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus. This is not the case in the instant application. There is no evidence that the single disclosed species is representative of the genus; there are no defined hybridization conditions (see rejection under 112/2nd paragraph) and there is no evidence that the necessary common attributes or features of the elements possessed by the members of the genus are present.

Applicant asserts that the Declaration of Dr. Spurlock in the parent application does not relate to bovine leptin, but rather to differences between leptin of different species. This point is noted, but it still does not detract from the statement of Dr. Spurlock that the "bottom line is that you do not know the bovine leptin sequence until you have the bovine leptin sequence". Given the bovine leptin sequence of SEQ ID NO:3, how can one predict any other bovine leptin sequence? How can one envision any other bovine leptin sequence without knowing where the regions of 100% homology occur within the sequences. Dr. Spurlock's statements regarding knowing or contemplating the exact sequence of a leptin gene in another species are just as relevant to the issue of predicting additional leptin genes in a single species.

Applicant argues at page 15 of the response that Dr. Spurlock did not "indicate what he means by functionality" and that the Examiner's conclusion is "purely speculative and therefore meaningless". Applicant's argument has been considered, but not found persuasive. The term "functionality" is being given its ordinary meaning - a thing is functional if it works and not functional if it doesn't work. The specification uses the term "functional derivative" as well as the latest Declaration under 1.131 wherein Applicant asserts that the 450 bp clone is a "functional derivative, functional variant". If the Examiner's conclusion is purely speculative and meaningless, Applicant will need to provide clarification as to what functional means if the assumed meaning is incorrect.

Applicant believes claims 13-30 and 39-51 that were in the present application when the present Office Action issued do satisfy the written description requirement, despite the Examiner's rejection of claims 13-30 and 39-51 under the written description requirement of the first paragraph of 35 U.S.C. §112. However, as noted above, Applicant has cancelled claims 13-30 and 39-51 for reasons unrelated to the Examiner's written description rejection of claims 13-30

and 39-51. Consequently, the Examiner's enablement rejection of claims 13-30 and 39-51 is moot.

Nonetheless, some clarifying comments about statements of the Examiner in support of the enablement rejection are provided herein. Applicants again emphasize the Examiner has taken the statement of Dr. Spurlock out context and inappropriately attributed a meaning to the text. Dr. Spurlock actually stated:

> But merely knowing the murine sequence along with the homology does not provide any guidance as to which particular nucleotides or condons differ between species. The bottom line is that you do not know the bovine leptin sequence until you have the bovine leptin sequence. Even then, you may have variations within the species because of the genetic diversity that exists within all species populations. (Spurlock 1.132 declaration, 01-18-01, 08/688,908, paragraph 6)

This language does not lend itself to the interpretation that one skilled in the art would not know or understand what constitutes a bovine leptin sequence in light of the present invention as the examiner stated:

> Even if one of ordinary skill in the art could use the disclosed polynucleotide sequence to hybridize to bovine polynucleotides, the skilled artisan would not know if they were in possession of bovine leptin as stated so clearly by the inventor himself. (page 4, final action 04-04-06)

Applicant is in actual possession of a bovine leptin genus. The genus of DNA sequences are unique from murine and human at positions 2, 5, 92, 131, 146, 147, 176, 182, 183, 225, 279, 280, 302, 311, 313, 322, 333, 340, 356, 368, 401, 404, 414, or 444 of SEQ ID NO: 3.

Claim Rejections Under the Enablement Requirement of the First Paragraph of 35 U.S.C. §112

In the Office Action, the Examiner rejected claims 13-30 and 39-51 under 35 U.S.C. §112, first paragraph, as allegedly failing to satisfy the enablement requirement:

> Claims 13-30, 39-51 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for the reasons of record.

Applicant argues that the Kennes article demonstrates that the scientific literature does indeed recognize nucleic acid molecules having at least about 20 bases of a nucleotide sequence derived from a leptin gene that encodes a leptin molecule. Applicant's argument has been considered, but is not persuasive. The issue the Examiner was raising was not directed to the meaning of the term "encode", but rather with the recitation that the encoded molecule be "leptin". The claims have been amended such that they do not read on a nucleic acid having 20 bases and the limitation of encoding a bovine leptin polypeptide. For clarity sake, the molecule of Kennes et al which "encodes leptin" is much longer than 20 bases. If leptin is roughly 145 amino acids long, it would require at least 435 nucleotides to encode for the protein. The molecules of Kennes et al. have many more nucleotides, based on the location of the polymorphisms found (i.e. positions 2845, 3996, 2728, 3469). Therefore, on its face, the specification does not teach a polynucleotide as short as 20 bases in length which also encodes bovine leptin. The claims previously recited "at least about 20", but the claims must be enabled for their full breadth, and the lower limit of 20 was not enabled. This argument is moot in light of the claim amendments which now include "and encodes at least a fragment", because 20 nucleotides could encode a fragment.

The claims are still not enabled for hybridization to at least about 20 bases or 50 bases and encoding a bovine leptin polypeptide. The lower limits of the claims are directed to hybridization to 20 nucleotides or 50 nucleotides. If only 20 nucleotides hybridize, the percent identity is roughly 4% identity. If only 50 nucleotides hybridize, the percent identity is roughly 11% identity. Considering that between species (human to bovine), there is conservation of approximately 88%, one of ordinary skill in the art would not reasonably expect conservation of only 4-11 % to provide for a polynucleotide that encodes a bovine leptin polypeptide. There are no examples of a single variant of bovine leptin in the instant specification, and there is a but (sic) a single example of a bovine leptin in the instant specification. While the skill in the art is high, there is no guidance or direction provided in the instant specification for making mutations or variations to the given coding sequence; there is no disclosure of which regions of the molecule should be conserved or which regions could be variable. Based on the teachings of the prior art, one might expect that the nucleic acid encoding bovine leptin could be varied to some degree (12% based on the conservation with the human protein), but would this molecule still be considered a "bovine" leptin? If the nucleic acid is not present in the cow, can it still be considered bovine leptin. Or if the starting material is from cow, and the molecule is mutated such that it now has the sequence of the human molecule, is it still considered "bovine" leptin? Regardless, the issue is that based on the lack of guidance in the specification and the prior art for only 4-11% identity to the given molecule, the

> lack of examples, and the degree of unpredictability in the art, the claims are not enabled for the full breadth of the claims, absent evidence to the contrary.

Despite the Examiner's comments, claims 13-30 and 39-51 that were in the present application when the present Office Action issued are enabled by the disclosure in accordance with the first paragraph of 35 U.S.C. §112. However, as noted above, Applicant has cancelled claims 13-30 and 39-51 for reasons unrelated to the Examiner's enablement rejection of claims 13-30 and 39-51. Consequently, the Examiner's enablement rejection of claims 13-30 and 39-51 is moot.

Claim Rejections Under the Second Paragraph, 35 U.S.C. §112

In the Office Action, the Examiner alleged Applicant's use of "at least about" to characterize the number of bases (length) of a molecule in claims 17 and 18 and to characterize the number of bases of a sequence to which a molecule hybridizes in claims 14-15 and 19-20 is indefinite. In support of this rejection, the Examiner alleged:

> Claims 14, 15, 17-20 are indefinite for the recitation "at least about" in conjunction with a number of nucleotides which are to hybridize for the reasons of record in the previous Office action. This recitation is indefinite because the lower limits of what are to be encompassed by the claims are not clear. The instant specification does not indicate what range "at least about" is meant to encompass. Furthermore, "at least" is in direct conflict with "about" since "at least" sets a lower limit to the range, but "about" changes that limit. Therefore, the claims are indefinite because the metes and bounds of "at least about" cannot be determined.
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> Applicant argues this rejection at page 18 of the response. Applicant asserts that the term "at least about X" could alternatively be written as "about X or more" and "no one of ordinary skill in the art would be confused about the meaning of "at least about X". Applicant's argument has been fully considered but is not found to be persuasive. The phrase "at least" has a definite meaning; it sets a very definite lower limit for the number of nucleotides which are to hybridize. The term "about" is not specific to the precise number of nucleotides which are to hybridize. The use of the two phrases/terms together makes the claims indefinite because the metes and bounds of the number of nucleotides which are to hybridize cannot be determined. For example, does the claim encompass 15 nucleotides? Would 25 nucleotides be encompassed by "at least about 50"? Does the claim encompass 10 nucleotides? The skilled artisan would have no idea if

> they were infringing the claim because the metes and bounds are not clear and definite. The rejection is maintained for the reasons of record.

Despite the Examiner's allegations, claims, 14-15 and 17-20 that were in the present application when the present Office Action issued are believed definite in accordance with the second paragraph of 35 U.S.C. §112. However, as noted above, Applicant has cancelled claims 14-15 and 17-20 for reasons unrelated to the Examiner's indefiniteness rejection of claims 14-15 and 17-20. Consequently, the Examiner's indefiniteness rejection of claims 14-15 and 17-20 is moot.

Nonetheless, some clarifying comments about statements of the Examiner in support of the indefiniteness rejection are provided herein. The Examiner discounts Applicant's explanation about how the term "at least about X" could alternatively be written as "about X or more" without explanation. The Examiner counters with questions about whether 10 or 25 nucleotides would be encompassed by the term "at least about 50." Applicant previously admitted the "about 20" and the "about 50" portions of these terms are limited to minor variations from the base number (20 or 50 under the present facts). The answer to the Examiner's question is whether 10, or even 25, amount to minor variations from 50. Applicant suspects the Examiner realizes 10, or even 25, do not amount to minor variations from 50. Though the terms "at least about 20" and "at least about 50" are not exact, the indefinite query does not go to whether the subject terminology is exact. The Examiner has not produced any evidence demonstrating one of ordinary skill in the art would be unable to determine the scope of the terminology at issue.

Next, the Examiner alleged Applicant's use of the term "stringent hybridization conditions" in various claims allegedly renders claims 13-30 and 39-51 indefinite:

> Claims 13-30 and 39-51 are indefinite for the limitation of "stringent hybridization conditions". The limitation "stringent hybridization conditions" is equivalent to reciting a range without indicating the metes and bounds of the conditions since there is no indication of what conditions are to be encompassed by the claims. The specification does not provide a definition of what conditions are considered "stringent" and the art recognizes a multitude of conditions which could be used and considered "stringent". Because a multitude of conditions are encompassed by the claims, it is not clear which molecules which may hybridize under varying conditions are encompassed by the claims. New claims 50-51

> recite a variety of conditions and indicate that any of the conditions in any combination or all of the conditions are included. This still does not set forth a "set of conditions" by which the nucleic acid molecules will be isolated, therefore, there are still variables unaccounted for which will greatly affect which molecules will hybridize and which will not. Therefore, the metes and bounds of the claims are unclear and the claims are indefinite.
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> Applicant argues this rejection at pages 19-22. Applicant's arguments have been considered, but are not deemed to be persuasive. Applicant states that the use of broad terminology does not necessarily render a claim indefinite. Applicant is correct in saying that breadth does not equate to indefiniteness. However, this is not the case in the instant application. The metes and bounds of the claims cannot be determined because the claims encompass a wide host of molecules depending on which conditions are intended by the terminology "stringent hybridization conditions" and those skilled in the art would not know which conditions are intended by the claims because the metes and bounds of what is covered by the claims is unclear. In the absence of a true definition in the specification that indicates what conditions are intended by "stringent", the rejection is maintained for the reasons of record.

Despite the Examiner's allegations, Applicant does not believe use of the "stringent hybridization" terminology renders claims 13-30 and 39-51 that were in the present application when the present Office Action issued indefinite under the second paragraph of 35 U.S.C. §112. However, as noted above, Applicant has cancelled claims 13-30 and 39-51 for reasons unrelated to the Examiner's indefiniteness rejection of claims 13-30 and 39-51. Consequently, the Examiner's indefiniteness rejection of claims 13-30 and 39-51 is moot.

Nonetheless, some clarifying comments about statements of the Examiner in support of the indefiniteness rejection are provided herein. In support of the present rejection, the Examiner states "In the absence of a true definition in the specification that indicates what conditions are intended by 'stringent'", the rejection will be maintained. The issue is whether one of ordinary skill in the art would be able to reasonably understand the scope of the claim language, not whether there is an actual definition in the specification for all claim terminology. The Examiner's basis for alleging the stringent hybridization conditions terminology is indefinite is therefore clearly erroneous. A hard and fast definition is unnecessary if those of ordinary skill in the art would understand what is meant by stringent hybridization conditions. The Examiner

has not produced any evidence establishing that one of ordinary skill in the art would be unable to reasonably understand the scope of the stringent hybridization condition claim language. Therefore, the Examiner has effectively done nothing more than question the definiteness of the stringent hybridization condition claim language. This does not, however, establish that the subject claim language is in fact indefinite.

Furthermore, Applicant notes that nucleic acid hybridization, even as far back as 1989, was considered to be well understood:

> **Nucleic Acid Hybridization**
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> This is the most commonly used and reliable method of screening cDNA libraries for clones of interest. None of the other methods displays such an abundance of attractive features. Screening by nucleic acid hybridization allows extremely large numbers of clones to be analyzed simultaneously and rapidly, does not require that the cDNA clones be full-length, and does not require that an antigenically or biologically active product be synthesized in the host cell. **Furthermore, as a result of more than 20 years of work, the theoretical basis of nucleic acid hybridization is well-understood**. This has led to the development of a large number of different techniques that can accommodate nucleic acid probes of different lengths and specificities.

Sambrook, Joseph; Fritsch, Edward F.; Maniatis, Thomas; Molecular Cloning, A Laboratory Manual, Volume II, p. 8.46, Second Edition (1989) (Emphasis added; incorporated by reference in the priority application US 08/688908); attached as Exhibit A of this Amendment After Final.

The invention defined in the claims (now cancelled) that were rejected by the Examiner in the present Office Action belongs to the bovine leptin nucleotide genus and hybridizes to the nucleotide sequence of SEQ ID NO: 3 under stringent conditions. The Examiner is reminded the patent specification is not required to teach every detail in the related art because the specification is directed toward one of skill in the art "and preferably omits, what is well known in the art." Hybritech Inc. v. Monoclonal Antibodies, Inc., 802 F.2d 1367, 1384, 231 U.S.P.Q. (BNA) 81, 94 (Fed. Cir. 1986). Ira Donner in Patent Prosecution, Fourth Edition, Volume Two, p. 1515, states "[t]he Board of Patent Appeals and Interferences (Board) has further stated as follows":

> In rejecting a claim under the second paragraph of 35 USC 112, it is incumbent on the examiner to establish that one of ordinary skill in the pertinent art, when reading the claims in light of the supporting specification, would not have been able to ascertain with a reasonable degree of precision and particularity the particular area set out and circumscribed by the claims. Citing Ex Parte Wu, 10 USPQ2D 2031, 2033 (B.P.A.I. 1989) (citing In re Moore, 439 F.2d 1232, 169 USPQ 236 (C.C.P.A. 1971); In re Hammack, 427 F.2d 1378, 166 USPQ 204 (C.C.P.A. 1970))

Applicant points out that the comments recited above from Sambrook et al. establish a significant hurdle for the Examiner to establish a prima facie case that one of ordinary skill in the art would not ascertain with a reasonable degree of precision and particularity the invention defined by the subject claims. The Examiner has not presented any documentary evidence showing why one skilled in the art would not reasonably understand the scope of the "stringent hybridization condition" terminology. To the contrary, the Examiner states "the art recognizes a multitude of conditions which could be considered 'stringent'." Final Office Action, 04-06-06, page 10, 2nd paragraph. The Examiner thus admits one of ordinary skill in the art would understand the scope of the "stringent hybridization condition" terminology because for the art to recognize the existence of a multitude of satisfactory stringent conditions, they would necessarily need to understand the ultimate objective and thus the definition of stringent conditions. Sambrook's laboratory manual contains detailed descriptions of conditions for hybridization of oligonucleotide probes (p. 11.45), calculating or empirically determining melting temperatures (pp. 11.46, 11.55-11.57), and estimating effects of mismatched nucleotide pairs (p. 11.47). See Exhibit A of this Amendment After Final. Furthermore, based on the statement recited above from the April 2006 Final Action, the Examiner admits those of skill in the art at the time the priority application was filed knew "a multitude" of available stringent hybridization conditions. This further supports Applicant's contention that on of ordinary skill in the art would be able to determine if they fall within the scope of the claimed invention, and hence, would possess the skills and knowledge necessary to practice the invention as presented in the specification and defined in the subject claims. Applicant believes these documented facts establish "stringent hybridization conditions" were well understood in the art at the time the priority document was filed.

The sequence defined in the claims rejected in the present Office Action based on the "stringent hybridization terminology" establishes an isolated gene sequence species and defines the conditions necessary for identifying the scope of genus members. First, the disclosed sequence provides the necessary foundation for determining the conserved DNA, and more importantly non-conserved DNA, positions of the bovine leptin nucleotide genus when compared to the known human and mouse sequences. One of ordinary skill in the art would understand the metes and bounds of the claimed invention when read in light of the specification.

Additionally, the priority application of the present application contains Example II and Example III that explicitly state stringent hybridization conditions. Those of ordinary skill in the art, based on the explanations provided in Applicant's prior Declaration Under 35 U.S.C. §132, would recognize the conditions explicitly recited in Examples II and/or III, for example, could be employed anytime stringent hybridization conditions are specified in a claim to satisfy that "stringent hybridization condition" claim language.

The Examiner alleges the claims defining "stringent hybridization conditions and present as of issuance of the present Office Action were indefinite "because the claims encompass a wide host of molecules depending on which conditions are intended by the terminology 'stringent hybridization conditions'". Contrary to this stated proposition, as noted above, the Examiner stated, "the art recognizes a multitude of conditions which could be used and considered stringent." It is also important to note that the claims specify the DNA binds to the identified sequence of the different claims under stringent hybridization conditions, rather than defining a method that employs stringent hybridization conditions. As the Examiner has implicitly noted, and the passages cited from Sambrook detail, one of ordinary skill in the art will recognize the objective of the claimed invention and would have the knowledge to choose from a variety of conditions to obtain the stringent conditions required to obtain the appropriate final result.

For the above stated reasons, Applicant believes the Examiner did not establish a prima facie case of indefiniteness for stringent hybridization condition in the present Office Action. The Examiner did not demonstrate the multitude of conditions known to one skilled in the art would not produce the appropriate results defined in the subject claims. Applicant

respectfully suggests that an indefiniteness rejection based upon the "stringent hybridization condition" terminology is inappropriate in the face of Sambrook's articulation of the state of the art, without specific documentation that establishes one of ordinary skill in the art would not been able to ascertain with a reasonable degree of precision and particularity the particular area set out and circumscribed by the subject claims.

Next, the Examiner continues to allege that use of the "substantially all" terminology in claims 16, 21, 23, 24, 26, 28, and 29 renders claims 16, 21, 23, 24, 26, 28, and 29 indefinite:

> Claims 16, 21, 23, 24, 26, 28, 29 are directed to nucleic acid molecules (DNA, mRNA) which "hybridizes" to "substantially all" of the bases of a recited sequence. However, these claims are indefinite for the failure to indicate what is intended by the recitation "substantially all".
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> Applicant argues at pages 23-24 that "substantially all" is definite. Applicant's arguments have been carefully considered but have not been found to be persuasive. First, Applicant again refers to U.S. Pat. No. 6,756,484. Again, the Examiner will not comment on the prosecution of another application. This patent is not directed to nucleic acid molecules which hybridize to substantially all of the bases of a recited sequence. Therefore, it is not germane to the instant fact situation. Applicant's assertion of "differential treatment" is not supported by any facts of record.
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> The specification does not define "substantially all" and its use in conjunction with the indefinite "stringent hybridization conditions" clearly does not provide sufficient explanation of the metes and bounds of the claims. Applicant states that "the meaning of the term "substantially all" clearly means something less than "all," yet more than "half". Applicant has provided no basis in the specification for this conclusion or definition. Applicant may mean 50%-100%, but someone in the art may view "substantially all" to be 80-100% while another researcher may view this to be 90-100%. Because the specification fails to include a definition of "substantially all" it would be "purely speculative and therefore meaningless" to conclude that "substantially all" "clearly means something less than "all," yet more than "half"' (see Applicant's own arguments at page 15 of this response regarding placing definitions on a term used by another with no clear definition provided). Because the metes and bounds of what is being claimed is unclear, the claims are indefinite.

Despite the Examiner's allegations, Applicant disagrees that use of the "substantially all" terminology automatically renders claims 16, 21, 23, 24, 26, 28, and 29 that were in the present application when the present Office Action issued indefinite under the second paragraph of 35 U.S.C. §112. However, as noted above, Applicant has cancelled claims 16, 21, 23, 24, 26, 28, and 29 for reasons unrelated to the Examiner's indefiniteness rejection of claims 16, 21, 23, 24, 26, 28, and 29. Consequently, the Examiner's indefiniteness rejection of claims 16, 21, 23, 24, 26, 28, and 29 is moot.

Nonetheless, some clarifying comments about statements of the Examiner in support of the indefiniteness rejection are provided herein. The Examiner has not produced any evidence establishing that one of ordinary skill in the art would be unable to reasonably understand the scope of the "substantially all" claim language. Therefore, the Examiner has effectively done nothing more than question the definiteness of the "substantially all" claim language. This does not, however, establish that the subject claim language is in fact indefinite. The Examiner alleges that "Applicant may mean 50%-100%, but someone in the art may view 'substantially all' to be 80-100% while another researcher may view this to be 90-100%." Again, merely questioning the definiteness of the "substantially all" claim language with hypotheticals does not establish that the subject claim language is in fact indefinite.

Finally, the Examiner alleges that claims 13, 24, 25, 27-30, 43 and 45 suffer from an antecendent basis issue that renders claims 13, 24, 25, 27-30, 43 and 45 indefinite:

> Claims 13, 24, 25, 27-30, 43 and 45 were rejected for reciting the article "a" in place of "the" when referring to the sequence represented by a sequence identifier. This is indefinite when referring to a single sequence because reference to a specific sequence would require the use of the article "the". The use of "a" implies that there are multiple sequences to chose from or represented by the sequence identifier, which is not the case when referring to a specific sequence as one is when referencing a sequence identifier. Applicant asserts that the claims were definite in scope - this is a spurious argument with no reasoning to support it. Applicant refers to MPEP §2173.05(e) as the rationale for using "a" or "an" in place of "the". After reading this section of the MPEP, the Examiner can find no mention or suggestion for using the article "a" or "an" in place of "the". The Examiner's explanation appears to be on point. Applicant's amendment to the claims has obviated this ground of rejection.

As noted above, Applicant has cancelled claims 13, 24, 25, 27-30, 43 and 45 for reasons unrelated to the Examiner's indefiniteness rejection of claims 13, 24, 25, 27-30, 43, and 45. Consequently, the Examiner's indefiniteness rejection of claims 13, 24, 25, 27-30, 43, and 45 is moot.

Applicant notes that Applicant's reference to MPEP §2173.05(e) as the rationale for using "a" or "an" in place of "the" relied on MPEP §2173.05(e) as the argument. Therefore, the Examiner's characterization of Applicant's argument as spurious is without basis. Furthermore, Applicant again directs the Examiner to MPEP §2173.05(e) that does mention and suggest using the article "a" or "an" in place of "the" in appropriate circumstances, the Examiner's comments notwithstanding:

> A claim is indefinite when it contains words or phrases whose meaning is unclear. The lack of clarity could arise where a claim refers to "said lever" or "the lever," where the claim contains no earlier recitation or limitation of a lever and where it would be unclear as to what element the limitation was making reference.

Claim Rejection Under 35 U.S.C. §102(a) Based on the Tellam Submission

In the Office Action, the Examiner rejected claims 25-30, 41-42, 45-49, and 50-51 under 35 U.S.C. 102(a) as allegedly being anticipated by Genbank ACC. No. U43943, Bos Taurus OBESE mRNA submission dated January 1996, hereinafter referred to as the "Tellam submission." Despite this rejection, Applicant continues to believe claims 25-30, 41-42, 45-49, and 50-51 that were in the present application when the present Office Action issued are allowable over the Tellam submission. However, as noted above, Applicant has cancelled claims 25-30, 41-42, 45-49, and 50-51 for reasons unrelated to the Examiner's rejection of claims 25-30, 41-42, 45-49, and 50-51 based on the Tellam submission. Consequently, the Examiner's rejection of claims 25-30, 41-42, 45-49, and 50-51 based on the Tellam submission is moot. Applicant's cancellation of claims 25-30, 41-42, 45-49, and 50-51 is in no way related to the Examiner's rejection of claims 25-30, 41-42, 45-49, and 50-51 under 35 U.S.C. 102(a) based on the Tellam submission.

Nonetheless, some clarifying comments about statements of the Examiner in support of the rejection based on the Tellam submission are provided herein. In the present Office Action, the Examiner provided the following additional comments regarding this rejection:

> Claims 25-30, 41-42, 45-49 and new claims 50-51 are rejected under 35 U.S.C. 102(a) as being anticipated by TELLAM et al. (Genbank Acc. No. U43943, Bos Taurus OBESE mRNA, 27 January 1996) for the reasons of record in the previous Office actions) (sic).
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> Applicant asserts that the Declaration under .37 CFR 1.131 is sufficient to overcome the instant rejection. MPEP 715.03(b) states that proof of prior completion of a species different from the species of the reference will be sufficient to overcome a reference indirectly under 37 CFR 1.131 if the species shown in the reference would have been obvious in view of the species shown to have been made by the applicant. After reviewing of (sic) the Declaration filed 16 December 2004, the nature of the "450 base pair clone" was understood. For the record, the description of the comparisons to be made by the Declarant were confusing. The nucleic acid molecule in Exhibit B is double stranded - the comparison to be made is with the bottom strand in the reverse orientation. Additionally, the markings over and the bases makes it very difficult to read. Regardless, it is clear that the "450 base pair clone" described is different from the nucleic acid molecule of the instant specification.
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> Applicant argues at page 26 of the response that based "on possession of one or both of these species, the question . . . is whether one of ordinary skill in the art would recognize that still other related species falling within the claims were in possession of the inventor [invention] prior to the effective date of the Tellam reference". Applicant's argument has been considered, but is not persuasive. This is not the question to be asked. MPEP 715.03 is very pointed as to what is required in order to antedate a reference under 102(a) directed to a species when the claims are directed to a genus:
>
> > The principle is well established that the disclosure of a species in a cited reference is sufficient to prevent a later applicant from obtaining a "generic claim." In re Gosteli, 872 F.2d 1008, 10 USPQ2d 1614 (Fed. Cir. 1989); In re Slayter, 276 F.2d 408, 125 USPQ 345 (CCPA 1960). Where the only pertinent disclosure in the reference or activity is a single species of the claimed genus, the applicant can overcome the rejection directly under 37 CFR

> 1.131 by showing prior possession of the species disclosed in the reference or activity. On the other hand, a reference or activity which discloses several species of a claimed genus can be overcome directly under 37 CFR 1.131 only by a showing that the applicant completed, prior to the date of the reference or activity, all of the species shown in the reference. In re Stempel, 241 F.2d 755, 113 USPQ 77 (CCPA 1957).
>
> Proof of prior completion of a species different from the species of the reference or activity will be sufficient to overcome a reference indirectly under 37 CFR 1,131 if the species shown in the reference or activity would have been obvious in view of the species shown to have been made by the applicant. In re Clarke, 356 F.2d 987, 148 USPQ 665 (CCPA 1966); In re Plumb, 470 F.2d 1403, 176 USPQ 323 (CCPA 1973); In re Hostettler, 356 F.2d 562, 148 USPQ 514 (CCPA 1966). Alternatively, if the applicant cannot show possession of the species of the reference or activity in this manner, the applicant may be able to antedate the reference or activity indirectly by, for example, showing prior completion of one or more species which put him or her in possession of the claimed genus prior to the reference's or activity's date. The test is whether the species completed by applicant prior to the reference date or the activity's date provided an adequate basis for inferring that the invention has generic applicability. In re Plumb, 470 F.2d 1403, 176 USPQ 323 (CCPA 1973); In re Rainer, 390 F.2d 771, 156 USPQ 334 (CCPA 1968); In re Clarke, 356 F.2d 987, 148 USPQ 665 (CCPA 1966); In re Shokal, 242 F.2d 771, 113 USPQ 283 (CCPA 1957).
>
> It is not necessary for the affidavit evidence to show that the applicant viewed his or her invention as encompassing more than the species actually made. The test is whether the facts set out in the affidavit are such as would persuade one skilled in the art that the applicant possessed so much of the invention as is shown in the reference or activity. In re Schaub, 537 F.2d 509, 190 USPQ 324 (CCPA 1976).

(1) While Applicant has provided proof of prior completion of a species different from the species of the reference, it is not sufficient to overcome the reference because the species shown in the reference would not have been obvious in view of the species shown to have been made by the Applicant. There is no suggestion

> to modify the "450 base pair clone" at any position in order to arrive at the molecule of Tellam. (2) Applicant may be able to antedate the reference indirectly, if the species completed by Applicant prior to the reference date provided an adequate basis for inferring that the invention has generic applicability. However, the disclosure of this additional species does not appear to satisfy this requirement because the evidence presented is not commensurate in scope with the claims. The true test is whether the facts set out in the affidavit are such as would persuade one skilled in the art that the applicant possessed so much of the invention as is shown in the reference or activity. In re Schaub, 537 F.2d 509, 190 USPQ 324 (CCPA 1976). There is no evidence that Applicant possessed the invention as is shown in the reference. Furthermore, the breadth of the claims is such that they encompass molecules which have only about 4-11 % identity to the disclosed nucleic acid molecule yet encode a bovine leptin polypeptide. The molecule of the "450 base pair clone" only differs from the molecule in the instant specification by about 3 base pairs - therefore, this clearly does not support the breadth of the generic claims.
>
> **The Declaration filed on 16 December 2004 under 37 CFR 1.131 is sufficient to overcome the Tellam reference for the reasons provided above.**

Emphasis added. As the Examiner noted in her comments provided in the June 16, 2004 Office Action in support of the anticipation rejection based on the Tellam submission:

> . . . applicant may be able to antedate the reference indirectly by, for example, showing prior completion of one or more species which put him or her in possession of the claimed genus prior to the reference's date.

The 131 Declaration submitted on December 16, 2004 illustrates that Applicant was in possession of a first species falling within the scope of claims at issue prior to the effective date of the Tellam submission. Additionally, Applicant was in possession of a second species, the species of SEQUENCE ID NO. 3, since the priority application the present application is based upon (U.S. Patent Application No. 08/688,908 (now U.S. Patent No. 6,297,027)) was filed less than one year after the effective date of the Tellam submission. Based on possession of one or both of these species, the question, analogous to the question central to the Written Description inquiry, is whether one of ordinary skill in the art would recognize that still other related species falling within the claims were in possession of the inventor prior to the effective date of the Tellam reference.

The answer to this question is yes. The claims and the application disclose use of stringent hybridization conditions. Such use of stringent hybridization conditions is known in the art to yield structurally similar molecules such that one of ordinary skill in the art would not expect substantial variation among species encompassed within the scope of the claims. Indeed, even just the disclosed species of SEQUENCE ID NO. 3 that the Examiner has acknowledged, considered along with the stringent hybridization conditions defined in the claims and the level of skill and knowledge in the art, are sufficient to allow the skilled artisan to recognize the inventor was in possession of the necessary common attributes or features of the elements possessed by the members of the genus prior to the effective date of the Tellam reference. This analysis dovetails with the analysis provided for analogous fact patterns in Examples 9 and 10 in the Synopsis of Application of Written Description Guidelines available at http://www.uspto.gov/web/menu/written.pdf. The foregoing comments demonstrate the inventor did in fact have possession of the invention of the present application, as presently defined in the claims of the above-identified application, prior to the effective date of the Tellam reference.

Claim Rejections Under 35 U.S.C. §103(a) Based on the Tellam Submission

In the Office Action, the Examiner rejected claims 13-24 under 35 U.S.C. 103(a) as allegedly being obvious in light of the Tellam submission. In support of this rejection, the Examiner alleged:

> Claims 13-24 are under 35 U.S.C. 103(a) as being unpatentable over TELLAM et al. (Genbank Acc. No. U43943, Bos taurus OBESE mRNA, 27 January 1996) for the reasons of record in the previous Office action(s).
>
> As stated previously TELLAM et al. disclose a nucleic acid molecule (mRNA) which is an allelic variant of SEQ ID NO:3 of the instant application. TELLAM et al. do not disclose single or double stranded DNA, an expression vector or plasmid comprising the DNA or a host cell transformed or transfected with the plasmid. However, at the time of the instant invention, it would have been prima facie obvious to one of ordinary skill in the art to use the mRNA molecule of TELLAM et al. to generate a DNA molecule, which could then be placed into an expression vector or plasmid, and then placed into a host cell for the purpose of propagating the nucleic acid, as well as for expression of the encoded protein of

the nucleic acid of TELLAM et al. One would be motivated to do this because TELLAM et al. identify the nucleic acid as encoding bovine obesity protein (a.k.a. leptin) and this protein is known to be valuable in regulation of weight in mammals. At the time of the instant invention, such methods and techniques were old and well-known in the art, as evidenced by the disclosure of the instant specification at pages 9-10, therefore, a reasonable expectation of success was also present.

Applicant argues at pages 27-28 that "the mere disclosure of the mRNA molecule in Tellam . . . does not teach or suggest the . . . transformation to the complementary cDNA molecule. That teaching or suggestion must necessarily come from outside the Tellam submission and apparently came by virtue of hindsight reconstruction". Applicant's argument has been considered, but is not persuasive. As pointed out previously, TELLAM et al. identified the mRNA molecule as encoding bovine obesity protein. With the mRNA, the skilled artisan has the necessary information to produce a recombinant protein encoding bovine obesity protein. The motivation to produce such a protein comes from the identification by TELLAM et al. that the protein is a leptin from cows and it was well known in the art at the time the invention was made that leptin was related to regulation of weight in mammals. The methods necessary to create expression vectors or plasmids and host cells are "conventional techniques" and available to those skilled in the art, as stated in the specification (page 10, lines 10-17). Therefore, a *prima facie* case of obviousness was made, and does not rely on hindsight reasoning, contrary to Applicant's assertion. Therefore, in response to Applicant's argument that the Examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the Applicant's disclosure, such a reconstruction is proper. See In *re* McLaughlin, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). The specification is not being used to make obvious the instant invention, but rather to establish that construction of vectors and host cells was conventional and well-known to those skilled in the art at the time the invention was made.

Applicant asserts at page 28 that the Declaration filed under 1.131 obviates the instant rejection. This argument is not persuasive for the reasons provide above.

Despite the Examiner's comments, the Tellam submission does not teach, suggest, disclose, or render obvious the invention of the above-identified application, as defined in claims 13-24.

Therefore, despite this rejection, Applicant continues to believe claims 13-24 that were in the present application when the present Office Action issued are allowable over the Tellam submission. However, as noted above, Applicant has cancelled claims 13-24 for reasons unrelated to the Examiner's rejection of claims 13-24 under 35 U.S.C. 103(a) based on the Tellam submission. Consequently, the Examiner's rejection of claims 13-24 under 35 U.S.C. 103(a) based on the Tellam submission is moot.

Nonetheless, some clarifying comments about statements of the Examiner in support of the rejection based on the Tellam submission are provided herein. For reasons analogous to those provided above in relation to the Examiner's .§102 rejection based on the Tellam submission, the present invention, as defined in claims 13-24 was in the possession of the inventor on or before December 26, 1995 and therefore prior to the effective date of the Tellam submission. Consequently, the Tellam submission does not render obvious the invention of the above-identified application, as defined in claims 13-24.

Claim Rejections Under 35 U.S.C. §103(a) Based On The Friedman Patent

In the Office Action, the Examiner rejected claims 21-30 and 39-51 under 35 U.S.C. 103(a) as allegedly being unpatentable over U.S. Patent N. 6,309,853 to Friedman et al. (subsequently referred to as the "Friedman patent"). In support of this rejection, the Examiner now states:

> Claims 21-30 and 39-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Friedman et al. (U.S. Pat. No. 6,309,853) for the reasons of record in the previous Office action(s) as applied to the previously filed claims.
>
> Applicant argues the rejection at pages 29-31 of the response. Applicant's arguments appear to be based on the premise that the bovine leptin of the instant application is functionally different from the human and mouse leptin of the prior art. However, the rejection is not one of anticipation, but rather that the human and mouse leptin of the prior art meet the limitation of being functional derivatives based on the disclosure of the instant specification at page 7. A ""functional derivative" refers to any "fragment", "variant", "analog", or "chemical derivative" of the bovine adipocyte polypeptide that retains at least a portion of the function of the bovine adipocyte leptin" (see page 7). Therefore,

Friedman et al. teach nucleic acid molecules which are "functional derivatives" and "derivatives" of the bovine leptin of the instant application and (sic) because they possess "at least a portion of the function of the bovine adipocyte leptin". Friedman et al. teach that the nucleic acid molecules encoding leptin could be used to isolate nucleic acid molecules encoding leptin from other species, specifically cows (see column 48, lines 41-57), contrary to Applicant's assertion that "the Friedman patent does not teach, suggest or disclose the invention of the above-identified application". The claims are broadly directed to isolated nucleic acids which encode bovine leptin - based on the known high degree of nucleic acid similarity of the leptin molecules across species (taught in Friedman), the known existence of a bovine leptin molecule (taught in Friedman), motivation to isolate nucleic acid molecules encoding bovine leptin (taught in Friedman) and known methods of isolation of nucleic acid molecules encoding leptin using one species as a probe (taught in Friedman), the invention as a whole would have been *prima facie* obvious in view of Friedman.

Applicant's arguments at pages 29-30 regarding specific activities of bovine leptin are noted, but do not avoid the rejection of record. The claims do not require these specific activities and the specification only requires "at least a portion of the function of the bovine adipocyte leptin". This function would include any function, such as binding to a leptin receptor, antigenicity, etc. Therefore, Applicant's arguments are not persuasive.

Applicant argues that "the Examiner switched horses and basically alleged Applicants could only consider functional properties disclosed for bovine leptin in the present application. This is an erroneous and overly restrictive view by the examiner." Applicant's arguments have been considered, but are not persuasive. The claims do not require the isolated molecule to encode a bovine leptin with any particular biological activity. If one of ordinary skill in the art used the polynucleotides of Friedman et al. to hybridize to bovine polynucleotides using the methods taught in Friedman et al., there is more than a reasonable expectation of success in isolating a bovine version of leptin, especially since Friedman already confirmed that there was a polynucleotide encoding leptin present in cows, absent evidence to the contrary.

Applicant argues at page 31 that the Examiner merely makes conclusions and does not properly reject the claims under 103. In response to Applicant's argument that the Examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge

> gleaned only from the applicant's disclosure, such a reconstruction is proper. See In re McLaughlin, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). Furthermore, the rejection was based on the disclosure of Friedman, the success Friedman had in isolating a different species of leptin while using another species as a probe, the disclosure that leptin existed in cows, and the specific statement of motivation in Friedman to isolate the molecules from other species, including cows, and the very methods necessary to achieve this goal. Applicant has not provided any evidence on the record that one of ordinary skill in the art could not follow the teachings and guidance in Friedman et al. to isolate nucleic acids encoding leptin in cows. The fact that the encoded protein has some very specific biological properties in the cow is interesting, but not persuasive for the reasons given above and does not avoid the rejection of record.

Despite the Examiner's allegations, the Friedman patent does not teach, suggest, disclose, or make obvious the invention of the above-identified application, as defined in claims 21-30 and 39-51. However, as noted above, Applicant has cancelled claims 21-30 and 39-51 for reasons unrelated to the Examiner's rejection of claims 21-30 and 39-51 under 35 U.S.C. 103(a) based on the Friedman patent. Consequently, the Examiner's rejection of claims 21-30 and 39-51under 35 U.S.C. 103(a) based on the Friedman patent is moot.

Nonetheless, some clarifying comments about statements of the Examiner in support of the rejection under 35 U.S.C. 103(a) based on the Friedman patent are provided herein. Consistent with the Examiner's observation, the Friedman patent does disclose murine and human leptin DNA sequences and polypeptides. Also, consistent with the Examiner's observation, the Friedman patent does not disclose any bovine leptin DNA (or mRNA) molecules or polypeptides. Furthermore, consistent with the Examiner's observation, the Friedman patent does not disclose any functional derivative or variant DNA (or mRNA) molecules that encode for bovine leptin polypeptide.

New Claims Added by Applicant

Applicant has added new claims 52-86.. New claims 52-86 do not add any new matter to the above-identified application. Support for new claims 52-86 is believed to exist throughout the above-identified application. Applicant respectfully requests consideration and allowance of new claims 52-86.

CONCLUSION

New claims 52-86 are believed allowable. Therefore, consideration and allowance of new claims 52-86 is respectfully requested. The Examiner is invited to contact Applicant's below-named attorney, Philip F. Fox, to facilitate allowance of the above-identified application.

Respectfully submitted,

Date: October 6, 2006

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